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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,459	11/07/2001	David L. Lewis	Mirus.030.03	3774
25032	7590	02/22/2006	EXAMINER	
MIRUS CORPORATION 505 SOUTH ROSA RD MADISON, WI 53719			GIBBS, TERRA C	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/007,459	LEWIS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 October 2005 and 28 November 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11 and 13-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11 and 13-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This Office Action is a response to Applicant's Amendment and Remarks filed October 24, 2005 and November 28, 2005.

Claim 12 has been canceled. Claims 11, 17, and 18 have been amended.

Claims 11 and 13-18 are pending in the instant application. It is noted that claim 13 is dependent on canceled claim 12. Incidentally, claims 14 and 17 are dependent on claim 13 and claim 18 is dependent on claim 17. Claims 13, 14, 17, and 18 have not been examined on the merits because no meaningful search can be conducted on these claims since they are dependent on a canceled claim.

Claims 11, 15, and 16 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Amendment***

Applicant's Amendment filed November 28, 2005 to comply with 37 CFR § 1.121(c) is acknowledged.

Applicant's Terminal Disclaimers filed October 24, 2005 are acknowledged and have been accepted.

### ***Priority***

The updated reference to priority in the first line of the specification is acknowledged.

In the previous Office Action mailed August 24, 2005, it was noted that the instant application has not been afforded priority to 09/450,315, filed 11/29/1999 since no support could be found for the term "siRNA" in this parent application.

In response to this statement, Applicants argue that a siRNA is a double-stranded oligonucleotide that causes inhibition of expression of a gene. Applicants contend that support for RNA and double-stranded RNA is provided in the priority document at column 6, lines 18-20, 35, and 36. Applicants argue that support for siRNA is inherently supported in the priority document.

**Applicant's arguments have been fully considered but are not found persuasive** because support for a double-stranded RNA does not inherently support siRNA. For example, the instant specification at page 5, lines 11-13, discloses "double-stranded RNA that is responsible for inducing RNAi is termed interfering RNA. The term siRNA means short interfering RNA which is double-stranded RNA that is less than 30 bases and preferably 21-25 bases in length". Given this specific definition of siRNA, the priority document doesn't support the term "siRNA" because it does not recite or even suggest a "short interfering RNA" nor does it recite or suggest the specific size limitation of the siRNA.

In summary, parent application 09/450,315, filed 11/29/1999 does not have support for the term "siRNA", inherently or otherwise. Given this lack of support, the instant claims have been afforded priority to provisional application 60/315,394, filed 08/27/2001, which is the earliest date that supports the term "siRNA".

### ***Claim Objections***

In the previous Office Action mailed August 24, 2005, claims 17 and 18 were objected to because of minor informalities. **These objections are moot** in view of Applicants amendment to the claims filed October 24, 2005. It is noted that claims 17 and 18 have been amended to depend from a canceled.

### ***Claim Rejections - 35 USC § 112***

In the previous Office Action mailed August 24, 2005, claim 18 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is moot** in view of Applicants amendment to the claims filed October 24, 2005. It is noted that claim 18 has been amended to depend from a canceled.

### ***Double Patenting***

In the previous Office Action mailed August 24, 2005, claims 11-17 were provisionally rejected under the judicially created doctrine of double patenting over claims 1-14 and 16-19 of copending Application No. 10/012,804. **The rejection is moot** against claims 13, 14, 17, and 18 in view of Applicants amendment to the claims filed October 24, 2005. It is noted that claims 13, 14, 17, and 18 have been amended to

depend from a canceled. **This rejection is withdrawn** against claims 11, 15, and 16 in view of Applicant's Terminal Disclaimer filed October 24, 2005.

In the previous Office Action mailed August 24, 2005, claims 11-17 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 3-8 and 11-14 of U.S. Patent No. 6,379,966 ('966). **The rejection is moot** against claims 13, 14, 17, and 18 in view of Applicants amendment to the claims filed October 24, 2005. It is noted that claims 13, 14, 17, and 18 have been amended to depend from a canceled. **This rejection is withdrawn** against claims 11, 15, and 16 in view of Applicant's Terminal Disclaimer filed October 24, 2005.

### ***Claim Rejections - 35 USC § 103***

In the previous Office Action mailed August 24, 2005, claims 11-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, A. (Methods, 1999 Vol. 18:286-295) in view of Elbashir et al. (Nature, 2001 Vol. 411:494-498) and Zhang et al. (Human Gene Therapy, 1999 Vol. 10:1735-1737). **The rejection is moot** against claims 13, 14, 17, and 18 in view of Applicants amendment to the claims filed October 24, 2005. It is noted that claims 13, 14, 17, and 18 have been amended to depend from a canceled. **This rejection is maintained** against claims 11, 15, and 16 for the reasons of record set forth in the previous Office Action mailed August 24, 2005.

### ***Response to Arguments***

In response to this rejection, Applicants argue that Zimmer et al. do not describe any functional activity of the oligonucleotide in the liver following tail vein injection. Applicants contend that instead, Zimmer et al. teach subcutaneous injection into an implanted tumor and describe no functional activity of the oligonucleotide in the liver following tail vein injection. Applicants point the Examiner to page 293 of Zimmer et al. Applicants argue that mere accumulation in the liver is insufficient to demonstrate functional delivery to the liver. Applicants argue that the instant specification demonstrates functional delivery of siRNA to cells *in vivo* as evidenced by the sequence-specific inhibition of gene expression.

Applicant's arguments have been fully considered but are not found persuasive because Zimmer et al. explicitly teach, "*In vivo* the biodistribution of the oligonucleotide nanoparticle complex resulted in targeting of oligonucleotides to the liver" (see Abstract). Further, Applicant is reminded that the claims do not recite any function activity of the oligonucleotide in the liver. Instead the claims are simply drawn to delivering a siRNA into a liver cell. While Applicants argue that the instant specification demonstrates functional delivery of siRNA to cells *in vivo* as evidenced by the sequence-specific inhibition of gene expression, this is irrelevant because the instant claims do not recite any function activity of the oligonucleotide in the liver following tail vein injection.

Applicants also argue that the claims have now been amended to indicate that increasing the permeability of the vessel is *within the target tissue*. Applicants contend

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that this is in contrast to Zimmer et al. where the pressure is limited to the point of the tail vein injection.

This argument has been fully considered, but is not found persuasive. At the outset it is noted that the instant specification does not define the term target tissue. Therefore, interpreted broadly, a target tissue includes a tail vein. The amendment to the claims to indicate that increasing the permeability of the vessel is *within the target tissue* does not obviate the instant rejection because Zimmer et al. teach delivering an antisense oligonucleotide complexed with positive and negative charged polymers into a liver cell following tail vein injection. It is the Examiner's opinion that the injection method disclosed by Zimmer et al. increases the permeability of the vessel within the tail vein (e.g. target tissue), since the needle used is external to the tail vein. Regardless of the fact that the pressure is limited to the point of injection as Applicants argue, the pressure is still within the target tissue (e.g. tail vein).

It is noted that the instant claims have been amended to recite "an efferent or afferent mammalian vessel". The tail vein used in the method of Zimmer et al. would appropriately be an efferent vessel since an oligonucleotide injected into the tail vein would be delivered outwardly to the liver, as demonstrated by Zimmer et al.

It would have been obvious at the time of filing to combine the teachings of Elbashir et al. and Zhang et al. with the teachings of Zimmer et al. to devise the method as instantly claimed.



Applicant's amendment necessitated the new grounds of rejection presented below:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 14, 17, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the limitation "the process of claim 12" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 12 has been canceled. Incidentally, claims 14 and 17 are dependent on claim 13 and claim 18 is dependent on claim 17. Claim 13 and claims 14, 17, and 18 that depend therein are rejected and have not been examined on the merits because no meaningful search can be conducted on these claims since they are dependent on a canceled claim and the metes and bounds of the claims cannot be determined.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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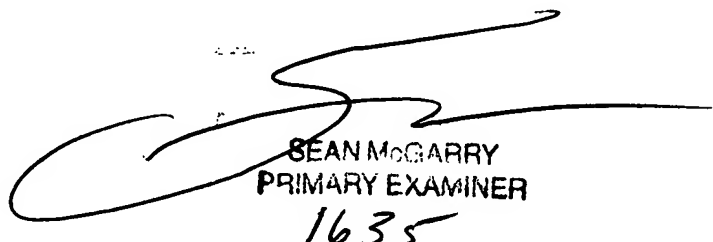
TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg  
February 6, 2006

  
SEAN MCGARRY  
PRIMARY EXAMINER  
1635